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Species Formed from R_2Mg and HMPA in Benzene[1]

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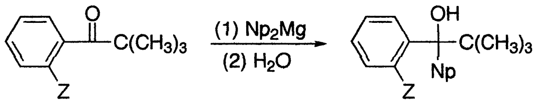
Summary: Solutions prepared in benzene from (neopentyl)$_2$Mg and HMPA exhibit NMR absorptions attributed to (neopentyl)Mg(HMPA)$_2^+$ and to (neopentyl)$_3$Mg$^-$ (equilibrating with (neopentyl)$_2$Mg). Absorptions for these ions are observed only for preparations having HMPA to (neopentyl)$_2$Mg ratios greater than ca. 0.5 and less than ca. 2.

Studies involving HMPA, a potent member of the family of polar aprotic solvents,[2] and organomagnesium compounds were already numerous 35 years ago.[3] Such studies have focused particularly on effects on product distributions of using HMPA either as the solvent or as an additive. We initially intended to investigate the effects of HMPA as an additive on rates of reactions with ketones, the most important substrates for organomagnesium compounds. Complications limited kinetic observations but led to NMR observations of HMPA−organomagnesium solutions that indicate the formation of specific HMPA-containing species.

Results and Discussion

Kinetic Observations. The system[4] used (eq 1)



(1)

1a Z = H
1b Z = CH$_3$

2a Z = H
2b Z = CH$_3$

offers several advantages for kinetic studies: (1) rates with many organomagnesium species are convenient to follow by monitoring (we used GC analysis) formation of addition product; (2) absence of β-hydrogens in the neopentyl (Np = $(CH_3)_3CCH_2$) group and of α-hydrogens in **1** precludes reduction or metalation of the ketone, pathways that in reactions of ketones with organomagnesium compounds often compete with addition; and (3) Np_2Mg is readily purified by sublimation and soluble in a range of solvents. The nonpolar and noncoordinating solvent benzene was used. To minimize complications due to reactions of organomagnesium species formed by addition (e.g., RMgOR′ in reactions of R_2Mg), we studied *initial* rates.

Table 1. Effect of HMPA on Initial Rate of Formation of 2b from Reactions of Np$_2$Mg and 1b in Benzene at 25.0 °C

[Np$_2$Mg], M	[**1b**], M	[HMPA]/[Np$_2$Mg]	10^6 k, s^{-1}
0.050	0.19	0	3.2[a]
0.050	0.19	1	5.1
0.050	0.19	2	0.0039
0.10	0.047	0	0.23[a]
0.10	0.047	1	4.6
0.10	0.047	2	0.0011

[a] Derived from the rate laws and constants in ref 4.

In the absence of HMPA, the initial rate of formation of addition product from **1** and Np_2Mg has been shown to be zero order in the reactant in excess and first order in the other reactant (the consequence of the reactants forming a complex and the transition state of the rate-determining step having the same composition as the complex).[4] We could not obtain the same degree of reproducibility when efforts were made to study rates of addition to **1b** at [HMPA]/[Np_2Mg] ratios near 1. It turned out that *two liquid phases* were sometimes present. Therefore efforts to determine kinetic orders were abandoned; the rates listed in Table 1 are simply observed initial rates of formation of **2b** at the particular concentrations used. The observations, although subject to the problem of two phases, indicate that one HMPA has only a modest effect on rate, but two HMPA's significantly slow addition.[5]

NMR Observations. Preparations in benzene-d_6 with HMPA/Np_2Mg ratios ca. 0.7−1.3 resulted in two liquid phases. Although NMR studies used concentrations > 0.1 M, two phases were noted even at lower concentrations and the relative amounts of the layers did not seem to decrease significantly with decreasing concentration but did seem to be sensitive to temperature. Separation of the layers was difficult because they were of similar density and easily formed emulsions. The bilayer samples become homogeneous upon addition of sufficient HMPA or Np_2Mg, and the resulting solutions have NMR spectra identical to those of preparations that initially had the same HMPA/Np_2Mg ratios. Because of the bilayer problem, the representative NMR data in Table 2 do not include data for HMPA/Np_2Mg ratios close to 1. Four sets of absorptions are listed: ^{31}P absorptions of HMPA and ^{1}H absorptions of HMPA, CH_2Mg, and $(CH_3)_3CCH_2Mg$. *Each set has two absorptions at some ratios and different sets have striking similarities.*

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(2) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; VCH: Weinheim, l988.

(3) Normant, H. *Angew. Chem., Int. Ed. Engl.* **l967**, *6*, 1046. Normant, H. *Bull. Soc. Chim. Fr.* **1968**, 791.

(4) Chubb, J. E.; Richey, H. G., Jr. *Organometallics* **2002**, *21*, 3361.

(5) Observations of reactions with **1a** and a reagent of composition[6] NpMgBr(THF) led to similar observations: 0.5 or 1 HMPA have only small effects, but 2 HMPA's lower rates by 3 orders of magnitude.

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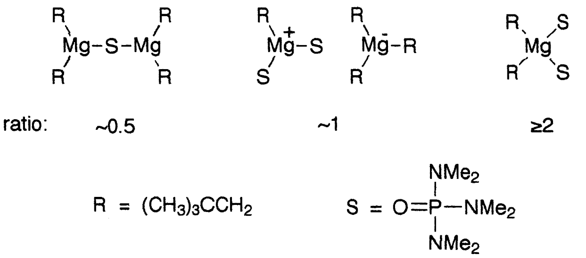
Table 2. Positions (Relative Intensities) of NMR Absorptions of Benzene-d_6 Solutions of HMPA and Np_2Mg

	^{31}P, δ[b]		^{1}H, δ[c]					
	HMPA		CH_3NP		$(CH_3)_3C$		CH_2Mg	
$S/[Np_2Mg]$[a]	$RMgS_2^+$	other	$RMgS_2^+$	other	$RMgS_2^+$	other	$RMgS_2^+$	other
0						1.21		0.25
0.49			2.10			1.42		0.32
0.59	24.9 (1)	27.8 (4.6)	2.27 (1)	2.14 (4.5)	1.33 (1)	1.42 (35)	−0.13 (1)	0.30 (67)
0.71	24.9 (1)	27.0 (1.05)	2.28 (1)	2.17 (1.1)	1.33 (1)	1.46 (13)	−0.13 (1)	0.31[d] (18)
1.26	24.9 (1)[d]	24.1 (0.51)	2.29	2.32[d,e]	1.31 (1)	1.56 (7.8)	−0.13 (1)	0.49 (~7)
1.69	24.9 (1)	23.8 (6.3)	2.28 (1)	2.35 (5.7)	1.30 (1)	1.55 (22)	−0.15 (1)	0.10 (25)
1.88	24.9 (1)	23.8 (36)		2.36		1.54		0.06
2.31		23.8		2.38		1.53		0.04
3.37		f		2.39		1.59		0.10
∞		24.4		2.41		1.21		0.25

[a] Reactant ratio (S = HMPA). Determined from intensities of CH_3N and $(CH_3)_3C$ absorptions. [b] Relative to external phosphoric acid (80% H_3PO_4). [c] Relative to internal C_6D_5H (δ 7.15). [d] Absorption is broad. [e] Broadness of absorption precluded meaningful integration. [f] Inadvertently not recorded.

Scheme 1. Principal Species at Different HMPA/Np_2Mg Ratios



Species in Solution. Scheme 1 shows a minimal set of species proposed to explain the observations. HMPA is an excellent coordinating agent for organomagnesium compounds.[2,7] At low HMPA/Np_2Mg ratios, it is reasonable that Np_2Mg makes maximal use of the available coordination, resulting in each HMPA molecule being coordinated by two Np_2Mg molecules. Coordination even by three Np_2Mg molecules perhaps is possible at HMPA/Np_2Mg ratios < 1/2.

At high HMPA/Np_2Mg ratios, a species making maximal use of the favorable HMPA-magnesium coordination is expected, most probably resulting in two HMPA molecules per Np_2Mg molecule.[8] Four is the most common coordination number for organomagnesium compounds, particularly when the attached groups are sterically demanding (as are neopentyl and HMPA).[9]

Several observations suggest that $NpMg(HMPA)_2^+$ is a major species at HMPA/Np_2Mg ratios around 1 (eq 2, R = Np). (1) A specific species at ratios between 0.5 and 2 is suggested by a set of relatively constant absorptions: ^{31}P δ 24.9 (P of HMPA) and ^{1}H δ 2.28 (H's of HMPA), δ −0.13 (CH_2Mg), and δ 1.32 ($(CH_3)_3CCH_2Mg$). We assign these absorptions to $NpMg(HMPA)_2^+$. (2) Formation of two liquid phases at HMPA/Np_2Mg ratios around 1 suggests that significant amounts of ions are present. Formation of two liquid phases is frequent when $RMg(macrocycle)^+$ cations and organomagnesate anions (eq 3) are formed in benzene.[10] In fact, such formation of two phases is a more general phenomenon, often observed with organometallic ions in aromatic solvents.[11] With $RMg(macrocycle)^+$ species, however, one phase ordinarily has been markedly denser than the other and contained essentially all of the ionic species. The phases here are similar in density; efforts, not completely successful, to separate them and determine the NMR spectrum of each suggest that they contain similar species, though in somewhat different ratios. (3) The position of the ^{1}H NMR absorption of CH_2Mg, significantly *upfield* from the CH_2Mg absorption of Np_2Mg, suggests a coordinated RMg^+ cation. The α-H absorptions of $RMg(macrocycle)^+$ cations[10,12,13] are significantly upfield from those of R_2Mg.[14] $NpMg(HMPA)_3^+$ appears from examination of models to be sterically feasible. The evidence, however, particularly the indication that its concentration must be maximal at an HMPA/Np_2Mg ratio of ca. 1 rather than 1.5, indicates that the principal cation is $NpMg(HMPA)_2^+$.

$$2\,R_2Mg + 2\,HMPA \rightleftharpoons RMg(HMPA)_2^+ + R_3Mg^- \qquad (2)$$

$$2\,R_2Mg + \text{macrocycle} \rightleftharpoons RMg(\text{macrocycle})^+ + R_3Mg^- \qquad (3)$$

The discrete set of NMR absorptions for the neopentyl group of $NpMg(HMPA)_2^+$ indicates that it does not exchange rapidly (relative to the NMR time scale) with neopentyl groups of other species in solution. That only one other set of neopentyl absorptions is seen, however, indicates that the neopentyl groups of other species in

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(7) Lindsell, W. E. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, l982; Chapter 4. Lindsell, W. E. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, l995; Vol. 1; Chapter 3.

(8) In solutions with high HMPA/Np_2Mg ratios, the positions of the HMPA absorptions are so close to those of uncoordinated HMPA that the NMR observations do not rule out the possibility that exchange between coordinated and uncoordinated HMPA could be somewhat slow on the NMR time scale.

(9) There is abundant evidence in crystalline solids: Bickelhaupt, F. In *Grignard Reagents: New Developments*; Richey, H. G., Jr., Ed.; Wiley: Chichester, 2000; Chapter 9. Evidence in solution[7] now includes information from EXAFS and LAXS techniques: Ertel, T. S.; Bertagnolli, H. In *Grignard Reagents: New Developments*; Richey, H. G., Jr., Ed.; Wiley: Chichester, 2000; Chapter 10.

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(14) An upfield position, despite the formal positive charge of magnesium, can be considered to be the consequence of very strong coordination of the magnesium by effective electron donor atoms.

solution (e.g., Np_3Mg^-, Np_2Mg) do exchange rapidly. This is analogous to observations for solutions of R_2Mg and macrocycles (e.g., eq 3): besides absorptions for $RMg(macrocycle)^+$, only one other set of R absorptions is seen, even when excess R_2Mg must be present.[15]

Conclusions

$NpMg(HMPA)_2{}^+Np_3Mg^-$ is a major species at HMPA/Np_2Mg ratios near 1.[15] Two considerations suggest, however, that formation of these ions is only marginally favorable. First, they are not present significantly at ratios ≤ 0.5 nor ≥ 2. With limited HMPA, it is preferable not to form $NpMg(HMPA)_2{}^+Np_3Mg^-$ until the amount of HMPA exceeds that needed to convert all Np_2Mg to $(Np_2Mg)_2HMPA$. With sufficient HMPA, it is preferable to form $Np_2Mg(HMPA)_2$ rather than to have coexisting $NpMg(HMPA)_2{}^+Np_3Mg^-$ [16] and free HMPA. Second, similar ions were not observed in the most closely related study that we are aware of. Ducom studied ^1H NMR spectra of Et_2Mg in benzene to which HMPA was added.[17] Because of insolubility of Et_2Mg, observations were not made at HMPA/Et_2Mg ratios < 0.6. The difference between the positions of the ethyl CH_2 and CH_3 absorptions increased significantly between ratios of 0.6 and 2.0, with a probable inflection at a ratio of 1, but remained essentially constant at ratios > 2. Ducom did not report observing multiple ethyl absorptions at any ratio nor observing formation of a second phase. The principal differences from our study—ethyl rather than neopentyl groups and ^1H NMR observations at 60 MHz instead of 360 MHz—must be sufficient to change the outcome.

The kinetic observations indicate that solutions having an HMPA/Np_2Mg ratio of 1 react with **1** at rates not very different than do solutions having comparable concentrations of Np_2Mg.[18] This is consistent with observations that reactions of **1** with $NpMg(macrocycle)^+Np_3Mg^-$ and with Np_2Mg have relatively similar rates.[4,19] The slow rates of addition when HMPA/$Np_2Mg = 2$ are in accord with observations that effective O and N donor solvents generally decrease rates of formation of addition products from R_2Mg and ketones.[7]

Formation of $RMg(macrocycle)^+$ cations upon addition of some macrocycles to benzene solutions of R_2Mg and now observation of a coordinated RMg^+ cation upon addition of HMPA suggest that such cations may form at least in small amounts with other coordinating agents.[20]

Experimental Section

Procedures involving organometallic compounds were performed under a nitrogen atmosphere using Schlenk techniques, a glovebox, and a vacuum line. Nitrogen was purified by passing through columns of manganese oxide oxygen scavenger and molecular sieves (4 Å). Solutions for NMR analysis were prepared in the glovebox and transferred into NMR tubes to which an extension of routine glass tubing had been added to facilitate sealing with a flame. An NMR tube was capped temporarily with a septum, removed from the glovebox, immersed in liquid nitrogen, and sealed at the extension. NMR spectra were recorded at ca. 23 °C in benzene-d_6. ^1H NMR spectra were recorded at 360 MHz; absorption positions are relative to internal C_6D_5H (δ 7.15). ^{31}P NMR spectra were recorded at 145.8 MHz; absorption positions are relative to an external phosphoric acid (80% H_3PO_4) reference. Benzene and benzene-d_6 were distilled from CaH_2 and stored over molecular sieves under a nitrogen atmosphere. HMPA was distilled under reduced pressure over molecular sieves. Np_2Mg, **1a**, **1b**, **2a**, and **2b** were obtained as already described.[4]

Kinetic Experiments. Reactions were initiated by addition of an appropriate amount of a benzene solution of **1b** (1.0 M) and tetradecane (as a GC standard) to Np_2Mg and HMPA in benzene already in the reaction flask. The apparatus, procedure for removing and quenching aliquots, and GC analysis were as already described for solutions lacking HMPA.[4] Data were used only for formation of ≤6% of the limiting reactant. The plots of concentration of product versus time generally had $R^2 \geq 0.98$.

NMR Spectra of Np_2Mg−HMPA Preparations. The samples used to provide the data in Table 2 were prepared by addition of an appropriate amount of a 10% (w/w) solution of HMPA in benzene-d_6 to a solution of Np_2Mg (42 mg, 0.25 mmol) in sufficient benzene-d_6 to make the total volume 0.5 mL.

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[15] The results do not rule out the possibility that a dimer, $R_6Mg_2{}^{2-}$, rather than monomeric R_3Mg^- is a significant anionic species in the solutions if its alkyl groups are exchanging rapidly (e.g., by cleavage to R_3Mg^- followed by recombination). A dimer (two of the alkyl groups bonded to both Mg atoms) was found in the crystal structure[12] of a solid of composition $EtMg(2,2,1\text{-cryptand})^+Et_3Mg^-$.

[16] Organomagnesate anions such as Np_3Mg^- can coordinate with one O or N atom of an O or N atom donor.[10] In solutions having both Np_3Mg^- and Np_2Mg, however, it is likely that the limited amount of HMPA is coordinated principally to the latter.

[17] Ducom, J. *Bull. Soc. Chim. Fr.* **1971**, 3523. Also see: Ducom, J. *Bull. Soc. Chim. Fr.* **1971**, 3518. Evans, D. F.; Fazakerley, G. V. *J. Chem. Soc. A* **1971**, 184.

[18] Based on yields after a particular time, it was reported that the rate of formation of addition product from benzophenone and Me_2Mg in diethyl ether is increased only slightly by 1 equiv of HMPA (addition of ≥2 equiv of HMPA led to some precipitation). House, H. O.; Oliver, J. E. *J. Org. Chem.* **1968**, *33*, 929.

[19] The kinetic order with respect to the ketone of reactions of $Np(macrocycle)^+Np_3Mg^-$ (the macrocycle is 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane) and **1b** is not established; the comparisons here are of observed rates of formation of **2b** using comparable concentrations of reactants.

[20] ^1H NMR spectra of solutions of composition[6] (2-ethylbutyl)-$MgBr(THF)_2$ in benzene containing 2 or 3 equiv of TMEDA (but not of Et_3N) show a weak ^1H NMR absorption for CH_2Mg at δ −0.29, a position characteristic of coordinated RCH_2Mg^+ ions.